Comparison of Non-human Primate versus Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes for Treatment of Myocardial Infarction.

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Public Summary:
Non-human primates (NHPs) can serve as a human-like model to study cell therapy using induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs). However, whether the efficacy of NHP and human iPSC-CMs is mechanistically similar remains unknown. To examine this, RNU rats received intramyocardial injection of 1 × 107 NHP or human iPSC-CMs or the same number of respective fibroblasts or PBS control (n = 9–14/group) at 4 days after 60-min coronary artery occlusion-reperfusion. Cardiac function and left ventricular remodeling were similarly improved in both iPSC-CM-treated groups. To mimic the ischemic environment in the infarcted heart, both cultured NHP and human iPSC-CMs underwent 24-hr hypoxia in vitro. Both cells and media were collected, and similarities in transcriptomic as well as metabolomic profiles were noted between both groups. In conclusion, both NHP and human iPSC-CMs confer similar cardioprotection in a rodent myocardial infarction model through relatively similar mechanisms via promotion of cell survival, angiogenesis, and inhibition of hypertrophy and fibrosis.

Scientific Abstract:
Non-human primates (NHPs) can serve as a human-like model to study cell therapy using induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs). However, whether the efficacy of NHP and human iPSC-CMs is mechanistically similar remains unknown. To examine this, RNU rats received intramyocardial injection of 1 x 10(7) NHP or human iPSC-CMs or the same number of respective fibroblasts or PBS control (n = 9-14/group) at 4 days after 60-min coronary artery occlusion-reperfusion. Cardiac function and left ventricular remodeling were similarly improved in both iPSC-CM-treated groups. To mimic the ischemic environment in the infarcted heart, both cultured NHP and human iPSC-CMs underwent 24-hr hypoxia in vitro. Both cells and media were collected, and similarities in transcriptomic as well as metabolomic profiles were noted between both groups. In conclusion, both NHP and human iPSC-CMs confer similar cardioprotection in a rodent myocardial infarction model through relatively similar mechanisms via promotion of cell survival, angiogenesis, and inhibition of hypertrophy and fibrosis.